UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/662,783 | 09/12/2000 | Richard A. Shimkets | 15966-577 (CURA-77) | 3145 |

7590 12/05/2001

Mintz Levin Cohn Ferris
Glosky and Popeo P C
One Financial Center
Boston, MA 02111

| EXAMINER | |
|---|---|
| JIANG, DONG | |
| ART UNIT | PAPER NUMBER |
| 1646 | 4 |

DATE MAILED: 12/05/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application N . | Applicant(s) | |
|---|---|---|---|
| | 09/662,783 | SHIMKETS ET AL. | |
| | Examiner | Art Unit | |
| | Dong Jiang | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --*

**Peri d for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 September 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-65* is/are pending in the application.

4a) Of the above claim(s) *6-39 and 41-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-65* are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

**DETAILED OFFICE ACTION**

Applicant's election of Group I invention (claims 1-5 and 40), and SEQ ID NO:4 in Paper No. 5, filed on 17 September 2001, is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Accordingly, claims 6-39, and 41-65 are withdrawn from prosecution as being drawn to non-elected inventions.

Currently claims 1-65 are pending, and claims 1-5 and 40 are under consideration.

It is noted in the response that "applicants elect the species of SEQ ID NO:4". Applicants are advised that the election of a SEQ ID NO *is not* the species election, rather it is a restriction requirement, which is clearly stated at page 7 of the last Office Action, paper No. 4, filed on 17 July 2001.

***Formal Matters:***

Claims 1-5, and 40 are objected to for encompassing a non-elected subject matter, SEQ ID NO:2. The applicant is required to amend the claims to read only upon the elected invention.

***Objections and Rejections under 35 U.S.C. §101 and §112:***

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 and 40 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by a credible, substantial, or well-established utility.

Claims 1-5 and 40 are directed to an isolated polypeptide of SEQ ID NO:4, fragments, variants, and pharmaceutical composition thereof. Said polypeptide is a putative member of PDGF/VEGF family (page 14, the last paragraph), and designated FCTR2.

The specification discloses two polynucleotides (SEQ ID NO:1 and 3) encoding two polypeptides of SEQ ID NO:2 and 4 (FCTR1 and FCTR2), respectively. Both polypeptides seem to be members of PDGF/VEGF family, as the sequence analysis reveals that SEQ ID NO:2

has a likeness to VEGF-E (page 11, the last paragraph), and SEQ ID NO:4 shows similarity to FIGF (page 14, the last paragraph). The specification further asserts that a FCTRX is useful as a therapeutic agent in treating disorders such as those listed at page 5, lines 16-17, in promoting wound healing, neovascularization and tissue growth and regeneration needs (page 6, the second paragraph), for identifying cancerous cells as SEQ ID NO:1 is strongly expressed specifically in CNS cancer, lung, and ovarian cancers (page 5, the fourth paragraph), for generating antibodies useful as a therapeutic agnet (page 7, the second paragraph). Additionally, the specification provides examples demonstrating specific activities of the polypeptide of SEQ ID NO:2 (Examples 8-11). However, the asserted utilities for SEQ ID NO:4 (FCTR2) are not considered to be substantial or credible because all supporting evidence of the utilities is based on the studies of SEQ ID NO:2 (FCTR1), and there is no actual experiment result of any kind to confirm any function associated with FCTR2.

The statement in the specification that the similarities of the disclosed FCTR1 and FCTR2 polypeptides to previously described BMP-1 and VEGF-E polypeptides indicate a similarity of functions by the FCTRX nucleic acids and polypeptides of the invention (page 15, the first paragraph) is noted, and cannot be accepted in the absence of supporting evidence, because generally the art acknowledges that function cannot be predicted based solely on structural similarity to a known protein. For example, in the transforming growth factor (TGF) family, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF- family members BMP-2 and TGF-1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Additionally, Skolnick et al. (2000, Trends in Biotech. 18:34-39, see entire article, especially Box 2) states that knowing the protein structure by itself is insufficient to annotate a number of functional classes, and is also insufficient for annotating the specific details of protein function (see Box 2, p. 36). Doerks et al. (1998, Trends in Genetics 14:248-250) states that overpredictions of functionality occur because structural similarity often does not necessarily coincide with functional similarity. Smith et al. (1997, Nature Biotechnology 15:1222-1223) remark that there are numerous cases in which proteins having very different functions share structural similarity due to evolution from a common ancestral gene. Brenner (1999, Trends in Genetics 15:132-133) argues that accurate

inference of function from homology must be a difficult problem since, assuming there are only about 1000 major gene superfamilies in nature, then most homologues must have different molecular and cellular functions. Finally, Kopchick et al. (U.S. Patent 5,350,836) disclose several antagonists of vertebrate growth hormone that differ from naturally occurring growth hormone by ***a single*** amino acid (column 2, lines 37-48). Therefore, established utilities for known PDGF/VEGF members, or disclosed utilities for FCTR1 can not be automatically applied to the FCTR2 without functional analysis, especially for the fact that the sequence structure of FCTR2 differs significantly from that of FCTR1 which has 370 amino acids, whereas FCTR2 has 132, and their sequences resemble different members of the family. The other disclosed uses in drug development, detection assays, predictive medicine, and treatment (page 69, lines 18-22) based upon the utilities of other members of PDGF/VEGF family, or FCTR1 are not credible in the absence of knowledge of the functional tests, or any disclosed gene mutation, or any disease or condition which could be so detected, or treated.

Until some actual and specific biological significance can be attributed to the polynucleotide or polypeptide identified in the specification as FCTR2, one of ordinary skill in the art would be required to perform additional experimentation in order to determine how to use the claimed invention. Thus, there was no immediately apparent or "real world" utility and the claimed invention is incomplete as of the filing date.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, and 40 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a substantial or credible utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

In addition, even if there were utility and enablement of a protein having SEQ ID NO:4, enablement would not be commensurate in scope with the claims, which encompass variants no more than 15% different in amino acid sequence to that of SEQ ID NO:4 (as claims 1 and 40),

fragments of SEQ ID NO:4 (as claim 2), and variants of SEQ ID NO:4 with one or more conservative substitutions (as claim 5), which have no upper limitations as to the number of substitutions.

The specification discloses *two* amino acid sequences with particularity, FCTR1 and FCTR2 with SEQ ID NO:2 and 4, respectively. No other FCTRX variants or fragments meeting the limitations of these claims were ever identified or particularly described. The specification does not teach how to use FCTR2 variants or fragments. Since a biological function of FCTR2 is not disclosed in the specification, and since one skilled in the art could not determine with a reasonable expectation of success what a biological function of FCTR2 would be, the skilled artisan would not be able to make FCTR2 variants or fragments, and test them for a biological activity, because one is not disclosed. Furthermore, the specification provides no guidance as to how the skilled artisan could use an inactive FCTR2 variant or fragment, as no functional limitation associated with the FCTR2 variants or fragments in the claims. Therefore, it would require undue experimentation to practice this invention as claimed, because the skilled artisan would have no reasonable expectation of being able to use the FCTR2 variants or fragments for any purpose stated in the specification.

Furthermore, even if there were utility and enablement of a protein having SEQ ID NO:4, claims 3 and 4 would be further rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claim limitation of claim 3 is directed to a naturally occurring allelic variant of SEQ ID NO:4. The specification discloses the polypeptide of SEQ ID NO:4. No other variants or SEQ ID NO:4 meeting the limitations of these claims were ever identified or particularly described. The skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v.*

*Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 4 is indefinite for recitation "wherein the variant is the translation of ...". It is suggested that the language "wherein the variant is *due to* the translation of ..." be substituted therefor.

***Rejections Over Prior Art:***

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Eriksson et al. (WO200027879, provided by applicants) discloses a human platelet derived growth factor, PDGF-D, which comprises the amino acid sequence 100% identical to SEQ ID NO:4 of the present invention (see computer printout of the search results).

NCI-CGAP discloses a polynucleotide sequence, Locus AA488780 (EST, August 1997), which share 100% to the polynucleotide sequence encoding amino acid residues 67-132 of SEQ ID NO:4 (see computer printout of the search results).

***Conclusion:***

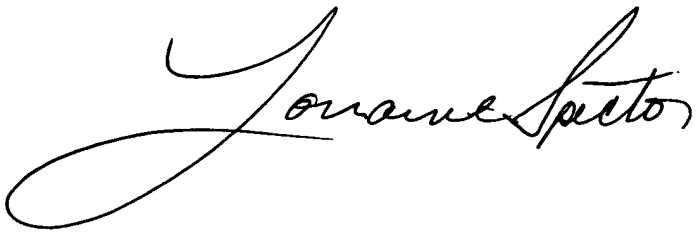
No claim is allowed.

***Advisory Information:***

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 703-305-1345. The examiner can normally be reached on Monday - Friday from 9:00 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, can be reached on (703) 308-6564. The fax phone number for the organization where this application or proceeding is assigned is 703-308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



LORRAINE SPECTOR
PRIMARY EXAMINER

DJ
11/26/01